Evaluating a Therapy Article

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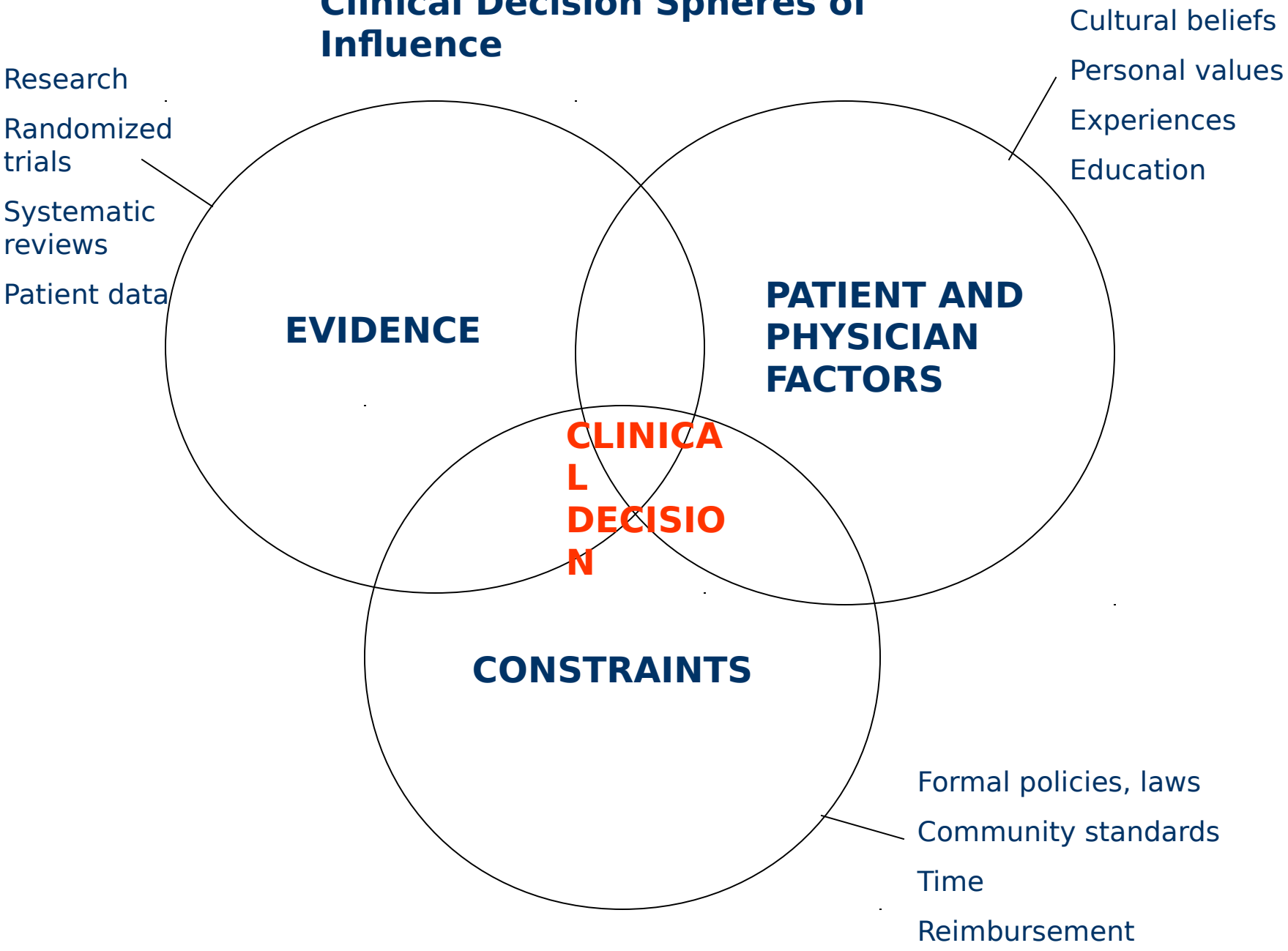
Clinical Decision Spheres of Influence



Roles of the Physician

- Prevention
- Diagnosis
- Treatment
- Prognosis

Treatment Article

"Zonisamide for Weight Loss in Obese Adults: A Randomized Controlled Trial"

FIRST THING: Determine ***Relevance***

Is this article worth taking the time to read?

Determine Relevance
(Based on the conclusion of the abstract)

- Did the authors study an outcome that patients would *care* about?
- Is the problem studied one that is *common* to your practice and the intervention feasible?
- Will this information, if true, require you to *change* your current practice?

Determine Validity

- Population
- Study Design
- Study Conduct
- Study Results

Population

- Are the studied patients similar enough to your patients that you can apply the results in your practice?

This addresses the ability to generalize the results

(external validity)

Study design

Was it a controlled trial?

Were the subjects randomly assigned?

Randomization is the best protection against being mislead.

The value of randomization

- 32 controlled trials of anticoagulation in acute MI
- Results by type of study:

Study design

- Were steps taken to conceal the treatment assignment from study personnel entering patients into the study?

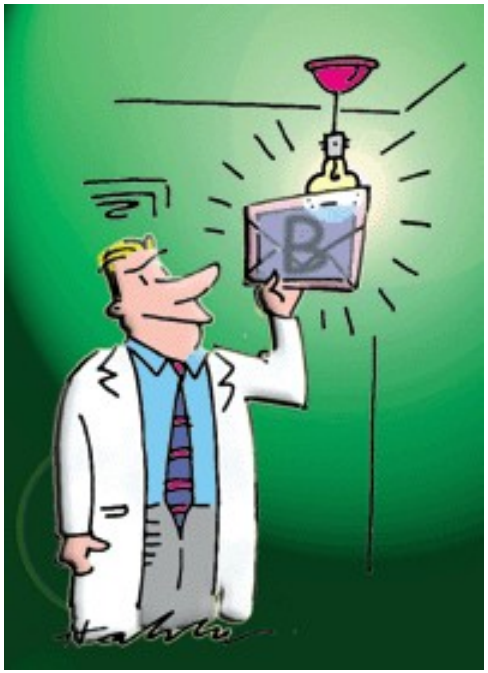
  “Concealed Allocation”

- Were patients and study personnel “blind” to treatment?

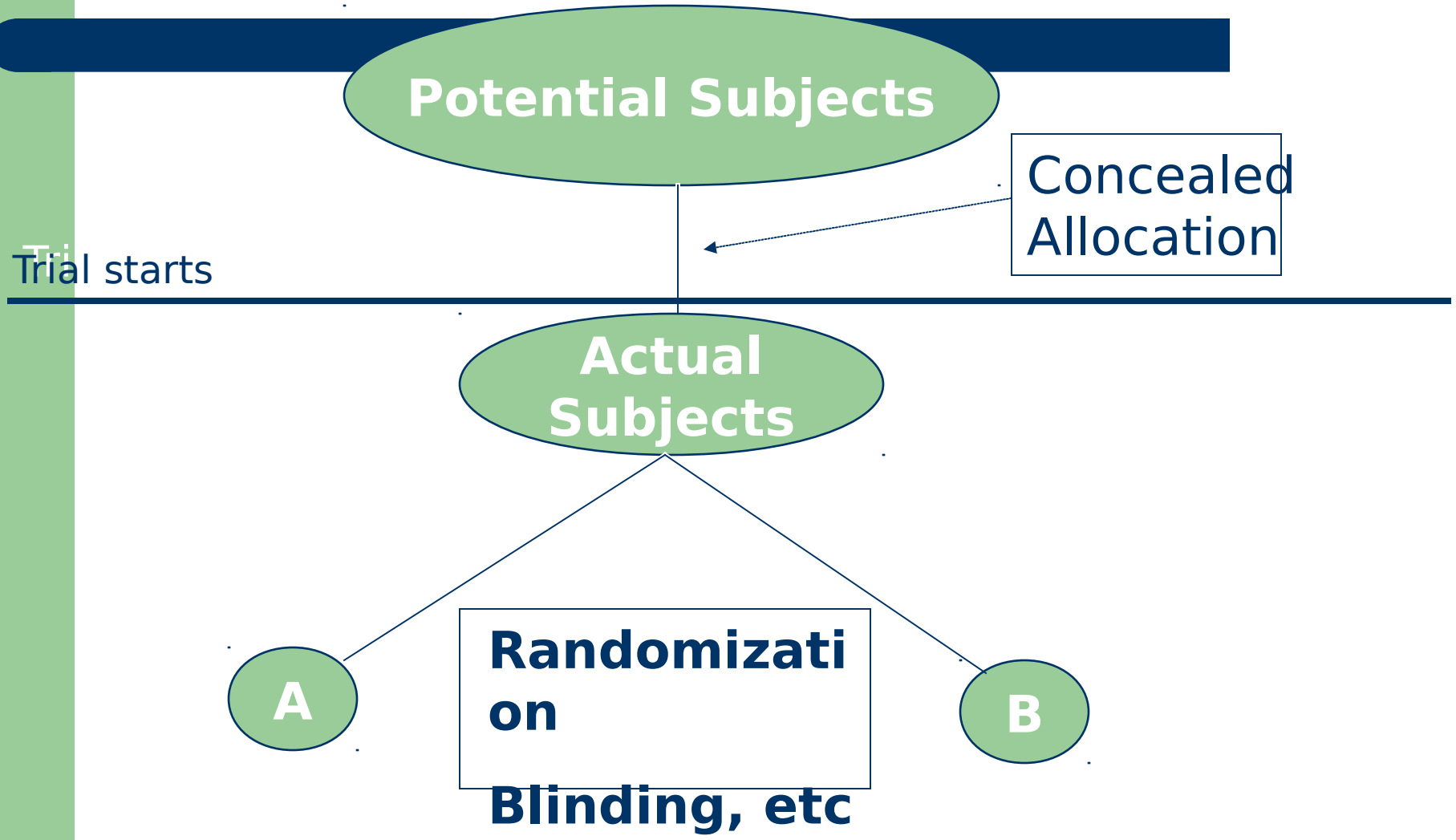
  Concealed Allocation ≠ Blinding

Was allocation assignment "concealed"?

Did investigators know to which group the potential subject would be assigned before enrolling them?



Conducting a Study



Importance of concealed assignment

- Meta-analysis of trials evaluating screening mammography
  - In studies in which allocation wasn't concealed
    - Higher SE status, education level in screened group
    - Uneven dropout rate due to pre-mammogram physicals (breast lumps)
    - Age disparity (avg 6 mo older in unscreened group)
  - Trials with concealed allocation = screening harmful!
    - No effect or increased mortality
    - 20% more mastectomies

Lancet Jan 8, 2000; Oct 20, 2001

Study conduct

- Were all patients who entered the trial properly accounted for at its conclusion?

  -Was follow-up complete?

  -Were patients analyzed in the groups to which they were randomized (“intention-to-treat” analysis)?
- Were the intervention and control groups similar? (Table 1)

Intent-to-treat

Should not compare

“compliers”

vs

“compliers” and “non-compliers”

Compliant subjects will always do better overall

Study results

- What were the results?
- Are the results clinically as well as statistically significant?
- If a negative trial, was the power of the study adequate?
- Were there other factors that might have affected the outcome?
- How will it change your practice?

Evaluating a Diagnostic article

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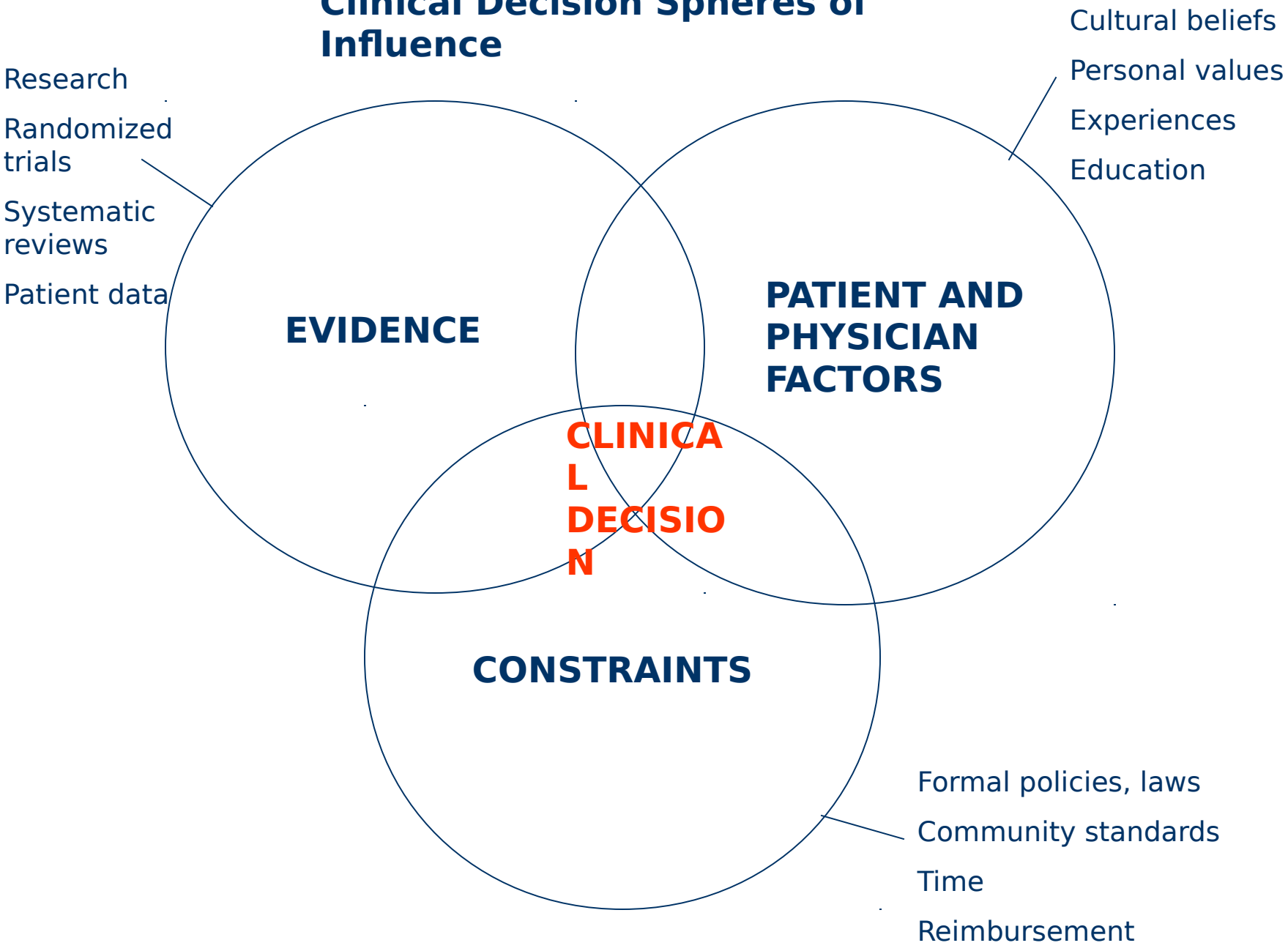
Clinical Decision Spheres of Influence



Roles of the Physician

- Prevention
- Diagnosis
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Evaluating Articles about Diagnostic Tests

GOALS:

- Understanding that diagnostic tests deal with probabilities, not certainties
- Distinguishing the *technical* accuracy of a test with the *clinical* accuracy of a test
- How the *prevalence* of the disease to improves or worsens a test

You must be able to deal with…

…Uncertainty!

“Physicians can do more to admit the existence of uncertainty, both to themselves and to their patients. Although this will undoubtedly be unsettling, it is honest, and it opens the way for a more intensive search for ways to reduce uncertainty.”

DAVID M. EDDY, MD, PhD

Technical vs. Clinical Accuracy

- “Baby Jeff”: The case of screening for muscular dystrophy
- Technical Accuracy of CPK test:
  - Sensitivity: 100%
  - Specificity: 99.98%

BUT…

The prevalence of MD is 1 in 5000 (0.02%)

Does Baby Jeff have M.D.?

Of 100,000 males, 20 will have M.D.

(1 in 5,000, or 0.02% prevalence)

- The test will correctly identify all 20 who have the disease (sensitivity = 100%)

Does Baby Jeff have M.D.?

- Of the 99,980 without M.D.
  - Specificity = 99.98%
  - 99,980 x 0.9998 = 99,960 will be negative
  - Therefore, false positives = 20

“. . . The Rest of the Story”

Therefore,

- Out of 100,000 infants, 20 will be truly positive and 20 will be false positive
- Positive predictive value = 50%

The child with a positive screening test only has a 50/50 chance of actually having MD

Technical vs. Clinical Accuracy

- Sensitivity: GIVEN disease, the probability of a positive test
- Specificity: GIVEN no disease, the probability of a negative test
- Positive Predictive Value: GIVEN a positive test, the probability of disease
- Negative Predictive Value: GIVEN a negative test, the probability of no disease

Predictive Values (Clinical Accuracy)

- Positive Predictive Value:

Influenced greatly by specificity and prevalence

- Negative Predictive Value:

Influenced greatly by sensitivity and prevalence

“Positive results, even for a very specific test, when applied to patients with a low likelihood of having the disease, will be largely false positives”.

Think of tests as enriching the prevalence of disease among people with positive tests.

$$LR+ = \frac{\text{Sensitivity}}{1\text{- Specificity}}$$

Sensitivity=90% Specificity=90%

LR+ = 9

(PRE TEST ODDS) X (LR+) = POST TEST ODDS

Prevalence = 1% Pre Test Odds = 1/99 Post Test Odds = (1/99) (9) = 9/99

PPV = Post Test “Prevalence” = 9/(99 + 9) = 9/108 = 8.3%

Diagnosis Article

"A Prospective Study of a Hand-held Ultrasound Device in Abdominal Aortic Aneurysm Evaluation"

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- Is the problem studied one that is *common* to your practice and is the test available to you?
- Will this information, if true, require you to *change* your current practice?

Determine Validity

- Description of the test
- Study Population
- Test Characteristics

Description of the test

- Is the new test reasonable? What are its limitations?
- Is the reference (gold) standard appropriate?
- Did all participants receive both the new test and the reference test?
- Were the results of the test interpreted without knowledge (blinded) of the reference test result and vice versa?

Study Population

- Were the patients enrolled randomly or consecutively?
- Does the study population generalize to your practice?

Test Characteristics

- What are the sensitivity, specificity and predictive values of the test?
- Calculate the prevalence of disease in the study.
- How does this compare to your practice?